

Guidance for HTLV-1 Screening and Confirmation in Potential Donors and Reporting Potential HTLV-1 Infection

Summary and Goals

On October 23, 2009, the OPTN/UNOS Executive Committee eliminated the requirement for pre-transplant deceased donor HTLV-1/2 testing, effective November 23, 2009. The basis for this decision included considerable organ wastage due to false positive results using screening tests, the very low prevalence of HTLV-1 in the United States, and the impending lack of availability of an FDA licensed HTLV-1 screening test that could practically be used in most Organ Procurement Organization (OPO) labs.

To assist members, the Ad Hoc Disease Transmission Advisory Committee (DTAC) was charged with creating a guidance document to assist the transplant community with ongoing testing issues and questions related to HTLV-1 in the organ transplant community. Since this resource is not considered OPTN policy, it does not carry the monitoring or enforcement implications of policy. It is not an official guideline for clinical practice, and it is not intended to be clinically prescriptive or to define a standard of care. This will not be used to determine member compliance with policy; rather it is a resource being provided to members for voluntary use.

HTLV background

Human T-cell lymphotropic Virus 1 (HTLV)-1 is a delta retrovirus endemic in the Caribbean, parts of South America, West Africa, Asia, and Oceania. In the Caribbean, 2-5% of adults are infected. In the United States (US), 0.035-0.046% of blood donors are infected with HTLV-1 or HTLV-2. Breast feeding is the most common form of transmission. Intravenous drug use, sexual intercourse, solid organ transplantation (SOT), and transfusion of cell-containing blood products (14.4-47.3% of recipients) may also result in transmission of infection.

HTLV-1 is associated with development of acute T-cell leukemia/lymphoma (ATL) in 2-5% of infected individuals and HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP) in a smaller percentage. Other inflammatory disorders have been associated with HTLV-1 and there is no reliably effective treatment. Most infected individuals have no clinical signs or symptoms of HTLV-1 infection. The effect of immunosuppression on progression from HTLV-1 infection to disease is unknown. No convincing evidence links HTLV-2 to human disease.

The true incidence of HTLV-1 in US organ donors is not well described, but appears to be very low (~0.03-0.5%). Proven transmission of HTLV-1 from donor to recipient has occurred in only one instance but with serious neurological impairment occurring in 3 seronegative recipients of one infected donor. Rapid development of HTLV-1 associated disease had been described in recipients seropositive prior to transplant; other case series with long term follow up demonstrate good outcomes in that circumstance. A review of the OPTN database of 162 recipients electively receiving HTLV-1/2 screen positive organs did not reveal any malignancy commonly associated with HTLV-1. This review, however, was limited by lack of confirmatory testing in the donor and absence of surveillance for neurological disease.

Circumstances in which HTLV donor screening may be performed

While the OPTN has removed the requirement for pre-transplant donor screening, some OPOs may elect to continue routine donor screening, to screen potential living donors, or to perform

targeted screening on donors perceived to be at higher risk of HTLV-1 infection. While the American Association of Tissue Banks (AATB) and the U.S. Food and Drug Administration (FDA) do not require testing of any but leucocyte rich tissues, there may be situations where testing of other tissue reveals donor infection.

Symptom driven testing in recipients

Given that universal donor HTLV-1 screening is no longer required for potential deceased organ donors, transplant centers should remain vigilant for clinical findings consistent with HTLV-1 associated disease. These findings would primarily include T-cell leukemia/lymphoma or otherwise unexplained neurological symptoms such as myelopathy. Testing in this circumstance should include both serological tests (with confirmatory testing) and nucleic acid based testing (*see below for specific tests*). Any positive HTLV-1 specific PCR results or confirmed positive serology for HTLV-1/2 antibodies suspected to be of donor origin should be reported to transplant programs receiving organs from the donor within 24 hours, as outlined in OPTN Policy 2.2.5. The potential transmission event must also be reported to the OPTN Patient Safety System per OPTN Policy 4.5.

Informing recipients of positive HTLV donor results

There are no proven monitoring or treatment guidelines for HTLV-1 exposures or infection, and the decision to inform recipients should be made by the physicians caring for the patient with the assistance of local transplant infectious disease (ID) experts if available. Secondary transmission to sexual partners or breast fed infants of recipients needs to be considered. Since most donors who screen positive are not infected with HTLV-1, recipients should not be informed of the donor screening result until a positive confirmatory test for HTLV-1 has been obtained (*see below for specific tests*). Positive confirmatory testing for HTLV-1 should be reported to transplant programs receiving organs from the donor within 24 hours, as outlined in OPTN Policy 2.2.5. The potential transmission event must also be reported to the OPTN Patient Safety System per OPTN Policy 4.5.

Management and monitoring of patients receiving organs or vessels from confirmed screen positive donors

The transplant team for recipients of confirmed HTLV-1 positive organs or vessels should consider working with local ID experts to develop a plan for evaluating recipients of organs from a donor who was **confirmed** to be infected with HTLV-1. As serological responses to infection may be attenuated by immunosuppression, nucleic acid based testing may be helpful in screening recipients. Nucleic acid based testing, however, may not be available in all locations. While there are currently no accepted guidelines for the evaluation and management of recipients of organs from HTLV-1 infected donors, if screening is considered at the local center, it is recommended that the recipient have (*see specific tests below*):

- HTLV-1/2 serology drawn as soon after donor infection is confirmed as a baseline in the recipient (if pre-transplant donor serum is available, this would be the preferred specimen) if they have not previously been screened for HTLV-1/2 infection (some centers do routinely perform HTLV-1/2 screening on all recipients).
- Consider HTLV-1 specific PCR and serology at 1, 3, 12 post-transplant (if available)
- Ongoing clinical monitoring for unexplained neurological disease and T-cell leukemia/lymphoma.

Reporting of recipients found to be HTLV-1 positive

All recipients found to be HTLV-1 positive for the first time (with possible donor-derived infection) post-transplant must be reported to the Improving Patient Safety portal as a potential donor-derived disease transmission per OPTN Policy 4.5:

<https://portal.unos.org/PatientSafety/Default.aspx?TRKR=hLso%2bnMAQsZnMS5ucz92zUH6KiXcxrac3xWIsE9tSrY7LbByFYiJJA%3d%3d>.

What specific test types are appropriate for HTLV-1/2 screening, monitoring and confirmation?

The Abbott PRISM HTLV-I/II assay is the only currently available FDA-licensed HTLV-1/2 screening test. Because most positive screening tests are false positives in a low seroprevalence population, any positive screening test (on either donor or recipient) should be confirmed.

Commonly used confirmatory tests include:

- Genelabs HTLV 2.4 (Western Blot)
- Innogenetics HTLV-I/II Line Immunoassay

As immunosuppression may reduce the immunological response to HTLV-1 infection, NAT testing (if available) should be performed on whole blood (not serum) as part of any monitoring strategy for recipients of seropositive organs. HTLV-1 may have low levels of viremia, and a negative NAT test does not exclude the possibility of HTLV-1 infection.

It is important to note that HTLV-1/2 screening assays do not distinguish between HTLV-1 and HTLV-2 infection. As HTLV-2 has not been convincingly associated with human disease, this distinction is critical. In most cases a determination between HTLV-1 versus HTLV-2 can be completed based on the banding pattern on confirmatory serological tests or by using NAT testing. It should be noted that none of the confirmatory or NAT tests are FDA-licensed for use and, and cannot be used for direct clinical purposes. In rare cases, it is not possible to determine if the patient has HTLV-1 or HTLV-2 using these methods; these individuals would be resulted as "indeterminate." Follow-up testing and expert consultation with the CDC may be required in this situation.

The FDA Vaccines, Blood and Biologics Tissue Safety & Availability web site

www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/TissueSafety/ucm095440.htm?sms_ss=email&at_xt=4d4af5ba7920b528%2C0#approved has current information regarding licensed assays for HTLV-1/2 screening as well as assays that may be cleared for patient testing but not licensed specifically for screening. It is important to note that research use only assays may be available but are not listed on the web site.

References

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Glynn SA, Kleinman SH, Schreiber GB, Busch MP, Wright DJ, Smith JW et al. Trends in incidence and prevalence of major transfusion-transmissible viral infections in US blood donors, 1991 to 1996. Retrovirus Epidemiology Donor Study (REDS). JAMA 284(2):229-235, 2000